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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,459	03/20/2001	Se-Jin Lee	JHU1170-2	8326

28213 7590 12/02/2003

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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/813,459	LEE ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on th cover she t with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *5-16* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/624,635.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 5-16 are pending.

The restriction between groups I and II in the paper mailed 12/16/2002 is withdrawn upon further consideration. Hence, Applicant's traversal of this requirement is moot.

Applicant's election with traverse of the species polyclonal antibodies, an enzyme label, and a Fab fragment of a polyclonal antibody in the paper filed 09/15/2003 is acknowledged. The traversal is on the ground(s) that there does not appear to be any basis provided for dividing the antibodies into species, particularly since "polyclonal antibodies" merely comprise a population of different "monoclonal antibodies, and there does not appear to be any need for different searches to be performed. Further, polyclonal antibodies and monoclonal antibodies share a "commonality of operation, function and effect" (see MPEP § 806.04(e)) with respect to the claimed invention in that they each specifically bind to a GDF-10 polypeptide. As such, it is submitted that the requirement to elect a species of antibody selected from polyclonal antibodies and monoclonal antibodies is improper and, therefore, respectfully requested that this requirement be removed. The species election with respect to the detectable label in claim 11 and claim 16 is traversed since all of the labels listed share a "commonality of operation, function and effect" (see MPEP § 806.04(e)) with respect to the claimed invention. Each of the labels recited in the claims provides a means for measurable detection of binding of an antigen binding molecule (e.g., antibody, Fab) to GDF-10 polypeptide as set forth in SEQ ID NO:5. As such, it is submitted that the requirement to elect a species of label is improper and, therefore,

respectfully requested that this requirement be removed. The species election with respect to the antibody fragment in claims 12 and 13 is traversed since both of these species are antigen binding molecules with binding specificity for GDF-10 polypeptide of SEQ ID N0:5 and therefore share a "commonality of operation, function and effect" (see MPEP § 806.04(e)) with respect to the claimed invention. Each of these antigen binding fragments, as well as an intact antibody, as claimed, bind to GDF-10 polypeptide as set forth in SEQ ID NO:5. As such, it is submitted that the requirement to elect a species of antibody fragment is improper and, therefore, respectfully requested that this requirement be removed. This is not found persuasive because for each antibody there are two species of antibody and two species of antibody fragments. For each antibody or antibody fragment there are 9 species of labels. In total there are 2 x (2 x 9) = 36 possible species. There is such a multiplicity of species that an unduly extensive and burdensome search is necessary. In any case, once a claim that is determined to be generic is allowed, all of the claims drawn to species in addition to the elected species which include all the limitations of the generic claim will ordinarily be obviously allowable in view of the allowance of the generic claim, since the additional species will depend thereon or otherwise include all of the limitations thereof.

The requirement is still deemed proper and is therefore made FINAL.

The application is not fully in compliance with the sequence rules, 37 C.F.R. § 1.821-1.825. Specifically, the specification fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. See page 26 and Figures 2, 3, 5. This is not meant to be an exhaustive list of places where the specification fails to comply with the sequence rules. The

specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The application cannot issue until it is in compliance. Nucleic acid sequences with 10 or more nucleotides, at least 4 of which are specifically defined, must comply with the sequence rules. Amino acid sequences with 4 or more residues, at least 4 of which are specifically defined, must comply with the sequence rules. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing." Applicant may bring the figure(s) into compliance by amending either the figure(s) or the "Brief Description of the Drawings" to recite the appropriate sequence identifier.

Correction is required.

Specification

Figures 2 and 3 are presented on separate panels. However, the brief description of the drawings refers only to Figure 2 and 3. If the drawings show Figures 1A, 1B, and 1C, for example, and the brief description of the drawings refers only to Figure 1, this is an error in the specification which must be corrected. See MPEP § 601.01(g). The Brief Description of the Drawings and the rest of the specification must be amended to accordingly.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. In the present case, the specific reference to the 08/624,635 prior application in the application data sheet does not include the relationship (i.e., *continuation, divisional, or continuation-in-part) between the applications.*

Correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for *patent by another filed in the United States before the invention by the applicant for patent, except that an* international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 5-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Smart (A) in view of Benjamini (U) and Kimball (V).

Smart discloses methods for determining the level of or a change in the level of a morphogen in a cultured cell using an antibody specific for the morphogen, e.g., in an immunoassay such as an ELISA or radioimmunoassay (column 3, full paragraph 3). BMP-3 is an example of a morphogen whose levels may be determined (paragraph bridging columns 3-4). In order to quantitate the production of a morphogenic protein by a cell type, an immunoassay may be performed to detect the morphogen using a polyclonal antibody specific for that morphogen (column 28, full paragraph 1).

The portion of the antigen that binds with the binding site of an antibody is termed an antigenic determinant or epitope. Various studies indicate that the size of an epitope is approximately equivalent to 5-7 amino acids. See Benjamini (U), page 40.

BMP-3, as disclosed by Smart (column 6, lines 25-32), comprises numerous epitopes that overlap the amino acid sequence of the present application's SEQ ID NO: 6, as indicated below:

```
; Patent No. 5650276
; GENERAL INFORMATION:
;   APPLICANT: SMART, JOHN
;   APPLICANT: OPPERMANN, HERMAN
;   APPLICANT: OZKAYNAK, ENGIN
;   APPLICANT: KUBERASAMPATH, THANGAVEL
;   APPLICANT: ROEGER, DAVID C.
;   APPLICANT: PANG, ROY H.L.
;   APPLICANT: COHEN, CHARLES M
;   TITLE OF INVENTION: MORPHOGENIC PROTEIN SCREENING METHOD
; INFORMATION FOR SEQ ID NO: 26:
;   SEQUENCE CHARACTERISTICS:
;     LENGTH: 104 amino acids
;     TYPE: amino acid
;     STRANDEDNESS: single
;     TOPOLOGY: linear
;   MOLECULE TYPE: protein
;   FEATURE:
;     NAME/KEY: Protein
;     LOCATION: 1..104
;     OTHER INFORMATION: /label= BMP3
US 08 278 729A-26

  Query Match             75.3%;  Score 434.5;  DB 1;  Length 104;
  Best Local Similarity   82.7%;  Pred. No. 7.9e-45;
  Matches   86;  Conservative   13;  Mismatches    4;  Indels    1;  Gaps    1;

Qy         18 CSRRYLKVDFADIGWNEWIISPKSFDAYYCAGACEFPMPKIVRPSNHATIQSIV-RAVGI 76
Db          1 CARRYLKVDFADIGWSEWIISPKSFDAYYCSGACQFPMPKSLKPSNHATIQSIVARAVGV 60

Cy         77 VPGIPEPCCVPDKMNSLGVLFLDENRNAVLKVYPNMSVETCACR 120
Db         61 VPGIPEPCCVPEKMSSLSILFFDENKNVVLKVYPNMIVESCACR 104.
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The fact that BMP-3 comprises numerous epitopes that overlap the amino acid sequence of the present application's SEQ ID NO: 6, indicates that Smart discloses a polyclonal antibody

that binds to a polypeptide comprising the amino acid sequence of SEQ ID NO: 6, as presently claimed. Such an antibody would also bind a polypeptide comprising the amino acid sequence of SEQ ID NO: 5 because SEQ ID NO: 6 is a subfragment of SEQ ID NO: 5. An antibody that binds BMP-3 in an immunoassay such as an ELISA, as taught by Smart, would comprise an antibody-enzyme conjugate that binds BMP-3, as indicated by Kimball (V) page 102.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6, 10, 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smart (A) in view of Benjamini (U) and Kimball (V) as applied to claim 6 above and further in view of Hornbeck (W).

Smart (A) in view of Benjamini (U) and Kimball (V) is discussed above and incorporated herein by reference.

This rejection is being made in the event of an argument or finding that an antibody that binds BMP-3 in an immunoassay such as an ELISA, as taught by Smart, would NOT comprise an antibody-enzyme conjugate that binds BMP-3.

Hornbeck teaches that an antibody-sandwich ELISA protocol using an enzyme-antibody conjugate specific for antigen is the most sensitive antigen assay (Table 2.1.1). Hornbeck does not teach an antibody that binds BMP-3 in an immunoassay such as an ELISA.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make an antibody that binds BMP-3 in an immunoassay such as an ELISA, as taught by Smart, and to modify that teaching by making an enzyme-antibody conjugate specific for antigen, as taught by Hornbeck, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because an antibody-sandwich ELISA protocol using an enzyme-antibody conjugate specific for antigen is the most sensitive antigen assay. The invention is prima facie obvious over the prior art.

Claims 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smart (A) in view of Benjamini (U) and Kimball (V) as applied to claims 5-11 above and further in view of Clark (X).

Smart (A) in view of Benjamini (U) and Kimball (V) is discussed above and incorporated herein by reference. Smart (A) in view of Benjamini (U) and Kimball (V) does not teach enzyme-Fab conjugate that binds BMP-3.

Clark teaches that a serious decrease in specificity may occur in the sandwich ELISA as a result of rheumatoid factor in the test sample. This non-specific effect can be eliminated by employing enzyme-labeled Fab. See page 177. Clark does not teach an antibody that binds BMP-3 in an immunoassay such as an ELISA.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make an antibody that binds BMP-3 in an immunoassay such as an ELISA, as taught by Smart, and to modify that teaching by employing enzyme-labeled Fab, as taught by Clark, with a reasonable expectation of success. One of ordinary skill in the art would

be motivated to make this modification in order to eliminate non-specific effects. The invention is prima facie obvious over the prior art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-8, 10-13, 15, 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to or encompass an antibody that binds a GDF-10. The term "GDF-10" encompasses a genus of polypeptides. Hence, these claims are genus claims. According to the specification, the term "GDF-10" encompass modifications of the GDF-10 primary amino acid sequence. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 5 or 6. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these

types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 5 or 6 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5-8, 10-13, 15, 16 are indefinite because they recite the term "GDF-10." Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "GDF-10" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claim 5 is indefinite because the antecedent basis for the term "fragments thereof" is unclear. It is unclear if the term refers to GDF-10 or the antibody. The metes and bounds are not clearly set forth.

Claims 9 and 14 are indefinite over the recitation of "has an amino acid sequence as set forth in SEQ ID NO: 5 or SEQ ID NO: 6" because the specification intends "all polynucleotides encoding all or a portion of GDF-10 are also included herein, as long as they encode a polypeptide with GDF-10 activity" and it is unclear if the GDF-10 polypeptide has "the" amino acid sequence as set forth in SEQ ID NO: 5 or SEQ ID NO: 6 or if the GDF-10 polypeptide comprises a portion of the amino acid sequence as set forth in SEQ ID NO: 5 or SEQ ID NO: 6. The metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 5 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 5, as written, does not sufficiently distinguish over antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by claim 6. See MPEP 2105.

Claims 5-16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The specification discloses that the invention provides a method for detecting a cell proliferative disorder of uterine or adipose tissue which comprises contacting an anti-GDF-10 antibody with a cell suspected of having a GDF-10 associated disorder and detecting binding to the antibody. The antibody reactive with GDF-10 is labeled with a compound which allows detection of binding to GDF-10. For purposes of the invention, an antibody specific for GDF-10 polypeptide may be used to detect the level of GDF-10 in biological fluids and tissues. An specimen containing a detectable amount of antigen can be used. A preferred sample of this invention is uterine or fat tissue. The level of GDF-10 in the suspect cell can be compared with the level in a normal cell to determine whether the subject has a GDF-10-associated cell proliferative disorder. Preferably the subject is human.

However, the specification does not disclose a specific up- or down-regulation of GDF-10 in a specific cell proliferative disorder. Further experimentation is necessary to attribute a utility to the protein and the claimed antibodies. Diagnosing an undisclosed or unspecified disease or condition clearly would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). The specification as filed does not disclose or provide any evidence that points to a specific activity for the protein and furthermore there is no art of record that discloses or suggests a specific activity for the claimed protein. Therefore there is no well-established utility.

Claims 5-16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

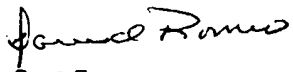
BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
NOVEMBER 30, 2003